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SUPPLEMENTARY MATERIAL

Title

Ventilatory function as a predictor of mortality in lifelong non-smokers: evidence from large British cohort studies

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e-Table 1

Descriptive characteristics of participants in the Health Surveys for England and Scottish Health Surveys, and in UK Biobank

<i>Characteristic</i>	<i>Smoking history</i>	<i>HSE-SHS age 40-69 at entry, white ethnicity</i>		<i>HSE-SHS age 70+ at entry, white ethnicity</i>		<i>UK Biobank age 40-69 at entry, white ethnicity</i>	
		<i>Males</i>	<i>Females</i>	<i>Males</i>	<i>Females</i>	<i>Males</i>	<i>Females</i>
Number of subjects included in Cox regression models	Never smokers	2343	4236	345	1084	56924	92419
	Former smokers	4768	4635	1624	1459	89542	102085
	Current smokers	3462	3178	517	392	19909	18605
Mean follow-up period (years)	Never smokers	13.75	13.93	12.26	13.03	6.52	6.54
	Former smokers	14.41	14.35	12.87	13.84	6.46	6.50
	Current smokers	14.46	14.11	13.39	13.52	6.47	6.54
All deaths	Never smokers	178	322	195	588	1143	1258
	Former smokers	757	455	1072	811	2714	1714
	Current smokers	732	539	406	260	1096	580
Respiratory deaths	Never smokers	10	14	26	84	41	28
	Former smokers	72	37	162	93	131	66
	Current smokers	80	69	87	53	69	37
Circulatory deaths	Never smokers	51	79	63	236	270	161
	Former smokers	272	118	415	330	668	192
	Current smokers	255	125	126	86	278	88
Cancer deaths	Never smokers	80	161	56	110	640	895
	Former smokers	290	219	283	165	1530	1232
	Current smokers	283	249	132	65	555	382
Other non-respiratory deaths	Never smokers	37	68	50	158	192	174
	Former smokers	123	81	212	223	385	224
	Current smokers	114	96	61	56	194	73

e-Table 2

Relationship of spirometric indices to mortality before and after 5 years among younger and older subjects, by smoking habit, in the Health Surveys for England and Scottish Health Surveys

<i>Timing of death</i>	<i>Smoking history</i>	<i>HSE-SHS age 40-69 at entry, white ethnicity</i>			<i>HSE-SHS age 70+ at entry, white ethnicity</i>		
		<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>	<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>
All deaths	Never smokers	6579 (500)	1.17 (1.09-1.25)	1.19 (1.10-1.28)	1429 (783)	1.24 (1.17-1.32)	1.22 (1.15-1.29)
	Former smokers	9403 (1212)	1.33 (1.28-1.39)	1.31 (1.25-1.37)	3083 (1883)	1.23 (1.19-1.28)	1.20 (1.16-1.25)
	Current smokers	6640 (1271)	1.30 (1.24-1.35)	1.20 (1.15-1.26)	909 (666)	1.36 (1.28-1.46)	1.23 (1.16-1.31)
Deaths within 5 years	Never smokers	6579 (103)	1.35 (1.17-1.56)	1.35 (1.16-1.57)	1429 (217)	1.37 (1.23-1.54)	1.38 (1.24-1.54)
	Former smokers	9403 (288)	1.43 (1.32-1.55)	1.49 (1.37-1.63)	3083 (590)	1.33 (1.25-1.41)	1.28 (1.20-1.36)
	Current smokers	6640 (332)	1.31 (1.21-1.43)	1.24 (1.15-1.35)	909 (250)	1.33 (1.20-1.48)	1.19 (1.08-1.32)
Deaths after 5 years	Never smokers	6476 (397)	1.12 (1.03-1.21)	1.14 (1.05-1.24)	1212 (566)	1.19 (1.11-1.28)	1.15 (1.07-1.24)
	Former smokers	9115 (924)	1.29 (1.23-1.36)	1.25 (1.19-1.32)	2493 (1293)	1.19 (1.14-1.24)	1.17 (1.12-1.22)
	Current smokers	6308 (939)	1.29 (1.23-1.36)	1.18 (1.12-1.25)	659 (416)	1.38 (1.27-1.50)	1.25 (1.15-1.36)

Spirometric indices (FEV1, FVC and FEV1/FVC ratio) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites. All hazard ratios are expressed per unit decrement in z-score, adjusted for age, sex, height, socio-economic status, geographical region and survey year.

e-Table 3 Relationship of spirometric indices to all-cause mortality before and after 5 years, among males and females, and among younger and older subjects, by smoking habit, in UK Biobank

Biobank age 40-69, white ethnicity, all usable spirograms

<i>Subjects and timing of death</i>	<i>Smoking history</i>	<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>
All subjects, deaths within 5 years	Never smokers	149343 (1599)	1.23 (1.17-1.28)	1.26 (1.20-1.32)
	Former smokers	191627 (2998)	1.40 (1.36-1.45)	1.40 (1.35-1.45)
	Current smokers	38514 (1112)	1.39 (1.32-1.46)	1.29 (1.22-1.36)
All subjects, deaths after 5 years	Never smokers	147744 (802)	1.18 (1.11-1.26)	1.21 (1.13-1.29)
	Former smokers	188629 (1430)	1.33 (1.27-1.39)	1.32 (1.25-1.38)
	Current smokers	37402 (564)	1.37 (1.28-1.47)	1.30 (1.20-1.40)
Males, all deaths	Never smokers	56924 (1143)	1.24 (1.18-1.31)	1.28 (1.21-1.35)
	Former smokers	89542 (2714)	1.39 (1.34-1.43)	1.39 (1.34-1.44)
	Current smokers	19909 (1096)	1.36 (1.30-1.43)	1.27 (1.21-1.34)
Females, all deaths	Never smokers	92419 (1258)	1.18 (1.12-1.24)	1.20 (1.14-1.27)
	Former smokers	102085 (1714)	1.37 (1.31-1.43)	1.34 (1.28-1.40)
	Current smokers	18605 (580)	1.42 (1.33-1.52)	1.33 (1.23-1.43)
Age 40-59 at entry, all deaths	Never smokers	90676 (872)	1.23 (1.16-1.31)	1.25 (1.17-1.33)
	Former smokers	101171 (1161)	1.36 (1.29-1.43)	1.37 (1.30-1.45)
	Current smokers	25584 (692)	1.39 (1.31-1.48)	1.27 (1.19-1.36)
Age 60-69 at entry, all deaths	Never smokers	58667 (1529)	1.20 (1.15-1.26)	1.23 (1.18-1.29)
	Former smokers	90456 (3267)	1.39 (1.35-1.43)	1.37 (1.33-1.42)
	Current smokers	12930 (984)	1.38 (1.31-1.45)	1.31 (1.24-1.39)
BMI<30kg/m ² , all deaths	Never smokers	113932 (1628)	1.17 (1.11-1.22)	1.19 (1.14-1.25)
	Former smokers	142418 (2893)	1.35 (1.30-1.39)	1.32 (1.27-1.37)
	Current smokers	29638 (1266)	1.37 (1.30-1.43)	1.27 (1.21-1.33)
BMI≥30kg/m ² , all deaths	Never smokers	33367 (696)	1.19 (1.11-1.27)	1.18 (1.10-1.27)
	Former smokers	46624 (1403)	1.36 (1.30-1.43)	1.37 (1.30-1.44)
	Current smokers	8326 (365)	1.49 (1.36-1.63)	1.44 (1.31-1.59)

Spirometric indices (FEV1 and FVC) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites.

All hazard ratios are expressed per unit decrement in z-score, adjusted for age, sex, height, socio-economic status and geographical region (recruitment centre).

e-Table 4

Comparison of best quality spiromgrams with all usable spiromgrams to predict all-cause and cause-specific mortality, by smoking habit, in UK Biobank

<i>Cause of death</i>	<i>Smoking history</i>	<i>Biobank age 40-69, white ethnicity, best spiromgrams</i>			<i>Biobank age 40-69, white ethnicity, usable spiromgrams</i>		
		<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>	<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>
All causes	Never smokers	102945 (1583)	1.23 (1.18-1.29)	1.29 (1.23-1.35)	149343 (2401)	1.21 (1.17-1.26)	1.24 (1.19-1.29)
	Former smokers	134173 (3043)	1.39 (1.35-1.44)	1.40 (1.35-1.45)	191627 (4428)	1.38 (1.35-1.42)	1.37 (1.33-1.41)
	Current smokers	26105 (1079)	1.39 (1.32-1.46)	1.30 (1.23-1.38)	38514 (1676)	1.38 (1.33-1.44)	1.29 (1.24-1.35)
Respiratory diseases	Never smokers	102945 (48)	2.07 (1.63-2.62)	2.22 (1.76-2.80)	149343 (69)	1.86 (1.53-2.27)	2.15 (1.77-2.61)
	Former smokers	134173 (140)	2.52 (2.20-2.88)	2.28 (1.98-2.63)	191627 (197)	2.46 (2.20-2.76)	2.26 (2.01-2.54)
	Current smokers	26105 (66)	2.93 (2.37-3.62)	2.44 (1.99-3.00)	38514 (106)	2.52 (2.15-2.96)	2.08 (1.76-2.45)
Circulatory diseases	Never smokers	102945 (269)	1.46 (1.31-1.62)	1.57 (1.41-1.76)	149343 (431)	1.41 (1.30-1.53)	1.47 (1.35-1.60)
	Former smokers	134173 (590)	1.56 (1.46-1.68)	1.66 (1.54-1.79)	191627 (860)	1.58 (1.49-1.67)	1.64 (1.54-1.74)
	Current smokers	26105 (219)	1.43 (1.28-1.60)	1.45 (1.28-1.63)	38514 (366)	1.41 (1.30-1.54)	1.38 (1.26-1.52)
Cancer	Never smokers	102945 (1023)	1.10 (1.04-1.16)	1.13 (1.07-1.20)	149343 (1535)	1.08 (1.03-1.13)	1.10 (1.05-1.15)
	Former smokers	134173 (1907)	1.27 (1.22-1.32)	1.25 (1.20-1.31)	191627 (2762)	1.25 (1.21-1.30)	1.23 (1.18-1.27)
	Current smokers	26105 (624)	1.27 (1.19-1.36)	1.18 (1.09-1.27)	38514 (937)	1.28 (1.22-1.36)	1.20 (1.13-1.27)
Other non-respiratory diseases	Never smokers	102945 (243)	1.44 (1.29-1.61)	1.51 (1.35-1.69)	149343 (366)	1.46 (1.33-1.59)	1.45 (1.32-1.59)
	Former smokers	134173 (406)	1.43 (1.31-1.56)	1.49 (1.36-1.63)	191627 (609)	1.41 (1.32-1.51)	1.43 (1.33-1.55)
	Current smokers	26105 (170)	1.36 (1.20-1.55)	1.25 (1.08-1.44)	38514 (267)	1.36 (1.23-1.51)	1.25 (1.12-1.39)

Spirometric indices (FEV1 and FVC) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites.

All hazard ratios are expressed per unit decrement in z-score, adjusted for age, sex, height, socio-economic status and geographical region (recruitment centre).

e-Table 5

Relationship of spirometric indices to all-cause and cause-specific mortality among younger and older subjects, by smoking habit, in the Health Surveys for England and Scottish Health Surveys

<i>Cause of death</i>	<i>Smoking history</i>	<i>HSE-SHS age 40-69 at entry, white ethnicity</i>			<i>HSE-SHS age 70+ at entry, white ethnicity</i>		
		<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>	<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>
All causes	Never smokers	6579 (500)	1.17 (1.09-1.25)	1.19 (1.10-1.28)	1429 (783)	1.24 (1.17-1.32)	1.22 (1.15-1.29)
	Former smokers	9403 (1212)	1.33 (1.28-1.39)	1.31 (1.25-1.37)	3083 (1883)	1.23 (1.19-1.28)	1.20 (1.16-1.25)
	Current smokers	6640 (1271)	1.30 (1.24-1.35)	1.20 (1.15-1.26)	909 (666)	1.36 (1.28-1.46)	1.23 (1.16-1.31)
Respiratory diseases	Never smokers	6579 (24)	1.72 (1.34-2.21)	1.61 (1.25-2.08)	1429 (110)	1.88 (1.58-2.24)	1.72 (1.45-2.03)
	Former smokers	9403 (109)	2.39 (2.08-2.76)	1.93 (1.67-2.24)	3083 (255)	1.72 (1.56-1.90)	1.56 (1.41-1.72)
	Current smokers	6640 (149)	2.29 (2.01-2.61)	1.77 (1.55-2.02)	909 (140)	2.27 (1.94-2.66)	1.68 (1.46-1.93)
Circulatory diseases	Never smokers	6579 (130)	1.21 (1.06-1.38)	1.22 (1.06-1.40)	1429 (299)	1.26 (1.13-1.39)	1.28 (1.16-1.41)
	Former smokers	9403 (390)	1.37 (1.28-1.48)	1.39 (1.28-1.50)	3083 (745)	1.20 (1.13-1.27)	1.22 (1.15-1.29)
	Current smokers	6640 (380)	1.26 (1.17-1.36)	1.22 (1.12-1.32)	909 (212)	1.21 (1.08-1.35)	1.20 (1.07-1.34)
Cancer	Never smokers	6579 (241)	1.10 (1.00-1.22)	1.12 (1.01-1.24)	1429 (166)	1.08 (0.95-1.23)	1.09 (0.96-1.24)
	Former smokers	9403 (509)	1.18 (1.10-1.26)	1.14 (1.06-1.22)	3083 (448)	1.19 (1.10-1.28)	1.14 (1.05-1.22)
	Current smokers	6640 (532)	1.21 (1.13-1.29)	1.09 (1.02-1.17)	909 (197)	1.20 (1.07-1.34)	1.08 (0.96-1.21)
Other non-respiratory diseases	Never smokers	6579 (105)	1.15 (0.98-1.34)	1.20 (1.03-1.41)	1429 (208)	1.11 (0.98-1.25)	1.04 (0.92-1.17)
	Former smokers	9403 (204)	1.22 (1.10-1.35)	1.32 (1.18-1.48)	3083 (435)	1.11 (1.03-1.20)	1.08 (1.00-1.17)
	Current smokers	6640 (210)	1.11 (1.00-1.24)	1.15 (1.03-1.28)	909 (117)	1.20 (1.03-1.40)	1.11 (0.95-1.29)

Spirometric indices (FEV1 and FVC) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites.

All hazard ratios are expressed per unit decrement in z-score, adjusted for age, sex, height, socio-economic status, geographical region and survey year.

e-Table 6 Spirometric prediction of mortality among subjects with and without a history of selected diseases at entry, by smoking habit, in UK Biobank

<i>Condition and cause of death</i>	<i>Smoking history</i>	<i>Biobank age 40-69, white, no history of condition</i>			<i>Biobank age 40-69, white, with history of condition</i>		
		<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>	<i>Total N (deaths)</i>	<i>zFEV1 HR (95%CI)</i>	<i>zFVC HR (95%CI)</i>
Respiratory disease at entry, all deaths	Never smokers	130798 (2081)	1.21 (1.16-1.26)	1.22 (1.17-1.27)	18545 (320)	1.23 (1.12-1.35)	1.33 (1.21-1.47)
	Former smokers	166259 (3711)	1.36 (1.32-1.40)	1.34 (1.30-1.38)	25368 (717)	1.48 (1.39-1.57)	1.48 (1.39-1.58)
	Current smokers	33491 (1352)	1.32 (1.26-1.38)	1.21 (1.15-1.27)	5023 (324)	1.53 (1.39-1.68)	1.48 (1.35-1.63)
Circulatory disease at entry, circulatory death	Never smokers	109141 (189)	1.40 (1.23-1.59)	1.40 (1.23-1.60)	40202 (242)	1.35 (1.20-1.51)	1.43 (1.27-1.60)
	Former smokers	131593 (281)	1.39 (1.26-1.54)	1.40 (1.26-1.57)	60034 (579)	1.59 (1.48-1.70)	1.64 (1.52-1.77)
	Current smokers	27843 (162)	1.32 (1.16-1.50)	1.29 (1.12-1.48)	10671 (204)	1.42 (1.26-1.59)	1.36 (1.20-1.54)
Cancer at entry, cancer death	Never smokers	137742 (978)	1.05 (0.99-1.11)	1.06 (1.00-1.12)	11601 (557)	1.10 (1.02-1.18)	1.13 (1.04-1.22)
	Former smokers	174917 (1898)	1.21 (1.16-1.26)	1.18 (1.13-1.23)	16710 (864)	1.32 (1.25-1.40)	1.30 (1.22-1.38)
	Current smokers	35573 (738)	1.29 (1.22-1.37)	1.18 (1.10-1.26)	2941 (199)	1.24 (1.11-1.39)	1.28 (1.12-1.45)

Spirometric indices (FEV1 and FVC) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites. All hazard ratios are expressed per unit decrement in z-score, adjusted for age, sex, height, area-based socio-economic measure and geographical region (recruitment centre)..

e-Table 7 Mortality from all causes, and from circulatory diseases, by quartile of systolic blood pressure, body mass index and spirometric indices among white lifelong non-smokers aged 40-69 at entry in national health surveys (HSE and SHS) and in UK Biobank

<i>Risk factor</i>	<i>Quartile</i>	<i>All-cause mortality</i>				<i>Circulatory mortality</i>			
		<i>HSE-SHS HR (95%CI)</i> <i>(based on 495 deaths)</i>		<i>Biobank HR (95%CI)</i> <i>(based on 2319 deaths)</i>		<i>HSE-SHS HR (95%CI)</i> <i>(based on 129 deaths)</i>		<i>Biobank HR (95%CI)</i> <i>(based on 403 deaths)</i>	
SBP	Q1 (low)	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
	Q2	0.80	(0.59-1.09)	0.93	(0.82-1.05)	1.20	(0.59-2.42)	0.81	(0.58-1.14)
	Q3	0.78	(0.58-1.06)	0.89	(0.78-1.01)	0.72	(0.34-1.50)	0.97	(0.71-1.34)
	Q4 (high)	1.12	(0.85-1.48)	0.99	(0.88-1.12)	1.98	(1.05-3.72)	1.12	(0.82-1.51)
BMI	Q1 (low)	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
	Q2	0.99	(0.75-1.30)	0.90	(0.79-1.01)	1.05	(0.59-1.87)	1.08	(0.77-1.51)
	Q3	1.05	(0.80-1.37)	0.95	(0.84-1.08)	1.39	(0.80-2.42)	1.35	(0.97-1.86)
	Q4 (high)	1.30	(1.00-1.68)	1.36	(1.21-1.53)	1.90	(1.13-3.22)	2.05	(1.51-2.79)
zFEV1	Q4 (high)	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
	Q3	0.95	(0.71-1.27)	1.12	(0.99-1.26)	1.73	(0.93-3.22)	0.97	(0.71-1.33)
	Q2	1.20	(0.91-1.58)	1.15	(1.01-1.30)	2.13	(1.16-3.89)	1.29	(0.96-1.73)
	Q1 (low)	1.56	(1.20-2.01)	1.60	(1.43-1.79)	2.24	(1.25-4.04)	1.99	(1.52-2.61)
zFVC	Q4 (high)	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
	Q3	1.01	(0.76-1.34)	1.05	(0.93-1.19)	1.38	(0.77-2.46)	1.16	(0.85-1.60)
	Q2	1.20	(0.92-1.58)	1.25	(1.11-1.41)	1.74	(0.99-3.04)	1.62	(1.20-2.18)
	Q1 (low)	1.66	(1.29-2.14)	1.62	(1.44-1.82)	1.98	(1.15-3.40)	2.19	(1.65-2.92)

Spirometric indices (FEV1 and FVC) are modelled as z-scores derived from the Global Lung Initiative 2012 reference equations for whites. All hazard ratios are adjusted for age, sex, height, socio-economic status, geographical region and survey year.